UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,802	11/02/2001	Michael D. Uhler	UM-06669	3812

7590 09/11/2003

Jaen Andrews
MEDLEN & CARROLL, LLP
Suite 350
101 Howard Street
San Francisco, CA 94105

EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/11/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,802	UHLER, MICHAEL D.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *14-24, 34-36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,25-33 and 37-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-42 are pending in the present application.

Applicant's election of Group I (claims 1-13, 25-33 and 37-42) with traverse in Paper No. 13 is acknowledged. Additionally, Applicant elects the following species: (a) "targeting molecules" as an additional complexing agent; and (b) "penton protein" as a species of a viral protein.

Applicant's response argues that the examiner has not met his burden of establishing that examining the claims of the three groups in a single application will create a serious burden on the PTO. The response argues that claims 14-24 of Group II are misclassified under class 436, subclass 518, and that they should be more appropriately classified under class 435. Applicant's response also argues that claims 34-36 of Group III are misclassified under class 435, subclass 4, entitled "Measuring or testing process involving enzymes or microorganisms; composition or test strip therefore; processes of forming such composition or test strip," whereas the claims are directed to a method of identifying a ligand of a receptor which method includes a transfection complex and a cell. Applicant's response further argues that the Examiner does not provide arguments showing separate inventive efforts by inventors, and that Groups I-III share the common element of a transfection complex comprising nucleic acid and first and second complexing agents. Lastly, Applicant's response argues that a different field of search has not been demonstrated for the different groups of inventions, and that considerable overlap is likely in the search for the claims in Groups

I to III. Applicant's arguments are respectfully found to be unpersuasive for the following reasons.

Firstly, Applicant is correct in pointing out that the claims of Group II should be more appropriately classified under class 435, rather than under class 436. More specifically, the claims of Group II should be classified under class 435, subclass 395 or 402 (solid support and method of culturing cells on said solid support). Due to the breadth of the claims, they can also be classified under class 424, subclasses 422 and 423 (implant or insert), for examples. This is because Applicant is clearly contemplating immobilizing a transfection complex on a surface, such as cellulose acetate membranes, to be implanted into solid tumors in whole organisms (see specification on page 70, first full paragraph). It should also be noted that a transfection complex immobilized on a surface is also utilized for screening purposes in a cell culture.

Secondly, claims 34-36 of Group III drawn to a method of identifying a ligand of a receptor protein are properly classified under class 435, subclass 4, which includes subclass 6 (involving nucleic acid). This is because a method of identifying a ligand of Group III is a testing process for identifying a ligand of a receptor protein, and it should be further noted that a receptor protein is also an enzyme (e.g., receptor kinases).

Thirdly, the inventions of Groups I-III are distinct each from the others as they are drawn to methods having different starting materials, method steps, desired end-results and therefore they require different technical considerations for achieving the end-results. For examples, the invention in Group I is drawn to methods of transfecting a cell comprising contacting the cell with a transfection complex immobilized on a surface;

whereas the invention of Group II is simply directed to a method for immobilizing nucleic acid to a surface without requiring any cell or any contacting or transfecting step; the invention of Group III is drawn specifically to a method of identifying a ligand of a receptor protein involving different starting materials from those of the inventions of Groups I-II (e.g., the transfection complex comprises first and second nucleic acids wherein said first nucleic acid encodes a receptor and said second nucleic acid encodes a protein, wherein said first and second nucleic acid are present in at least one expression vector. Additionally, the transfection complex of Group I is not required to form an array as it is in the method of Group II.

Fourthly, the search for each of the above inventions is not exclusively based on its classification in a Patent database, but also on other non-patent literature search databases.

Accordingly, because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, and separate search requirements, it would be unduly burdensome for the examiner to search and/or consider the patentability of all the inventions in a single application. Therefore, restriction for examination purposes as indicated is proper. This requirement is made **FINAL**.

Therefore, claims 14-24, 34-36 are withdrawn from further consideration because they are drawn to non-elected inventions.

Claims 1-13, 25-33 and 37-42 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 recites the limitation "wherein the membrane permeable molecule is a cationic lipid" in lines 1-2 of the claim. There is insufficient antecedent basis for this limitation in the claim. There is no recitation of any membrane permeable molecule in claims 27 and 25, upon which claim 28 is dependent.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9-12, 25, 27, 29, 32-33 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Pierce et al. (WO 97/49434).

Pierce et al. teach the preparation of a transfection complex comprising: (a) a heparin-binding moiety or a heparin-binding chimeric protein (e.g. an FGF-heparin binding domain conjugated chemically or as a fusion protein with PDGF or TGF-B will

bind a heparin-coated stent and a PDGF or TGF receptor, a cell surface receptor; see page 7, lines 19-24); (b) a nucleic acid binding domain (e.g., Poly-L-lysine, histones, protamines; see page 28, lines 22-35); and (c) a nucleic acid encoding a cytocide-encoding agent, wherein the component (a) is conjugated either by chemical linkage or as a fusion protein with the nucleic acid binding domain (page 25, lines 14-19). Pierce et al. also teach that cytoplasm-translocation signal sequence may be included in the heparin-binding moiety or a nucleic acid-binding domain, and membrane-disruptive peptides such as adenoviruses, virus-free viral proteins such as influenza virus hemaglutinin HA-2 may also be included in the conjugates to enhance gene delivery (page 40). The transfection complex is bound to medical devices (e.g., stents, tubing, probes, cannulas, catheters, vascular grafts, artifical heart valves) coated with or without heparin (page 57), and thereby the transfection complex is immobilized on a surface. Pierce et al. further teach that that the medical devices containing the transfection complex are to be implanted into an animal, and thereby contacting a cell with the nucleic acid in the transfection complex, to inhibit undesired cell proliferation or kill unwanted cells (e.g., to inhibit restenosis).

Accordingly, the teachings of Pierce et al. meet the limitations of the instant claims, and therefore Pierce et al. anticipate the instant claims.

Claims 25, 27 and 29-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al. (Proc. Natl. Acad. Sci. 87:3410-3414, 1990).

The claims are drawn to a transfection complex comprising nucleic acid and first and second complexing agents, said first complexing agent comprising a ligand for a receptor and said second complexing agent comprising a DNA binding molecule, the same with various other limitations in the dependent claims.

Wagner et al. teach the preparation of transferrin-polycation-DNA complexes, wherein the polycation is a small DNA-binding protein protamine or polylysines and that the polycation is covalently linked to transferrin through a disulfide linkage (see abstract).

Accordingly, Wagner et al. anticipate the instant claims.

Claims 25-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Ferkol, Jr. et al. (U.S. Patent No. 5,972,900).

Ferkol, Jr. et al. teach the preparation of a compacted gene delivery complex comprising: (a) a target binding moiety capable of binding to a polymeric immunoglobulin receptor present on the surface of a cell in a tissue of an animal (e.g., transferrin, albumin, glucagons and others, see col. 10); (b) a nucleic acid binding moiety (e.g., polylysine, histones, protamines and others, see col. 11); and (c) an expression vector comprising an oligonucleotide encoding one or more gene products, wherein the target binding moiety is conjugated to the nucleic acid binding moiety to form a carrier to couple with the expression vector (see Summary of the Invention). Ferkol, Jr. et al. further teach that the compacted or condensed gene delivery complex

can also be encapsulated using neutral lipids into liposome bodies or with cationic lipids to prolong in vivo expression (see col. 10, line 44 continues to line28 of col. 11).

Accordingly, Ferkol, Jr. et al. anticipate the instant claims.

Claims 25-27, 29-30 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Chroboczek et al. (WO 97/18317).

Chroboczek et al. teach the preparation of a composition comprising: (a) an adenoviral protein complex consisting of 12 pentons, each including at least one fiber and a penton base, but no other element from an adenovirus genome; (b) a transferrin/poly-L-lysine complex; and (c) a nucleic acid sequence, wherein the component (b) combines covalently or non-covalently with the nucleic acid sequence and the adenoviral protein complex (abstract and page 5, line 23 continues to line 9 of page 8). Chroboczek et al. also teach that the composition further comprises a pharmaceutically acceptable vehicle such as liposomes and others (col. 5, lines 15-24).

Accordingly, Chroboczek et al. anticipate the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 38-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chroboczek et al. (WO 97/18317) in view of Cheng (U.S. Patent No. 6,077,834).

Chroboczek et al. teach the preparation of a composition comprising: (a) an adenoviral protein complex consisting of 12 pentons, each including at least one fiber and a penton base, but no other element from an adenovirus genome; (b) a transferrin/poly-L-lysine complex; and (c) a nucleic acid sequence, wherein the component (b) combines covalently or non-covalently with the nucleic acid sequence and the adenoviral protein complex (abstract and page 5, line 23 continues to line 9 of page 8). Chroboczek et al. also teach that the composition further comprises a pharmaceutically acceptable vehicle such as liposomes and others (col. 5, lines 15-24).

However, Chroboczek et al. do not specifically teach a composition comprising a cationic lipid or lipofectamine.

At the effective filing date of the present application, Cheng already teach that cationic lipid or lipofectamine in a liposome formulation can be used in a delivery system for polynucleotides (DNA or RNA) to enter cells to exert their effects (see abstract and Summary of the Invention).

Accordingly, it would have been obvious for an ordinary skilled artisan to modify the composition taught by Chroboczek et al. by specifically utilizing a cationic lipid or lipofectamine as a pharmaceutically acceptable carrier because cationic lipid or lipofectamine has been successfully utilized in a delivery vehicle for polynucleotides into cells as taught by Cheng.

One of ordinary skilled artisan would have been motivated to carry out the above modification for the reason set forth above, which is cationic lipid or lipofectamine in a liposome formulation has been used successfully to deliver polynucleotides into cells as taught by Cheng.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-13, 25-33 and 37 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-13, 25-33 and 37 of copending Application No. 09/960454. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (703) 308-8339.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gerald Leffers, Jr., Ph.D., may be reached at (703) 305-6232, or SPE, Remy Yucel, Ph.D., at (703) 305-1998.

Quang Nguyen, Ph.D.

GERRY LEFFERS
PRIMARY EXAMINER